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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,909	02/13/2002	Nicole Chantel Barvian	A0000517-01-CFP	9232

28880 7590 11/03/2003

WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 11/03/2003

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s)

10/075,909

Examiner

Tamthom N. Truong

Applicant(s)

BARVIAN ET AL.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 1-5, 12-21, and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 6-10 and 22-24 is/are rejected.
- 7) ☒ Claim(s) 11 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,4,6. 6) ☐ Other:

DETAILED ACTION

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, and 12-18, drawn to method of inhibiting matrix metalloproteinase enzyme, and pharmaceutical composition comprising an MMP-13 inhibiting amount, classified in classes 514, and 544, various subclasses depending on substituents. Further restriction will be required if this group is elected.

II. Claims 6-11 (in part) and 22-24 (in part), drawn to compounds of formulae I-V with the following substituents:

R^4 and R^5 (independently) are **not** $(CH_2)_n$ heteroaryl, or they do **not** form a 3-8 membered ring optionally having additional heteroatoms of O, S, and/or N,

Or **Ar is aryl** (for formula V);

Also, method for treating inflammation, osteoarthritis, and rheumatoid arthritis using the above compounds.

classified in class 514, 544, various subclasses depending on substituents.

III. Claims 6-11 (in part) and 22-24 (in part), drawn to compounds of formulae I-V with the following substituents:

R^4 and R^5 (independently) are $(CH_2)_n$ heteroaryl, or they **form** a 3-8 membered ring optionally having additional heteroatoms of O, S, and/or N,

Or **Ar is heteroaryl** (for formula V);

Also, method for treating inflammation, osteoarthritis, and rheumatoid arthritis using the above compounds.

classified in class 514, 544, various subclasses depending on substituents. Further restriction will be required if this group is elected.

IV. Claims 19, 20, and 25, drawn to a method for treating cancer, classified in classes 514, and 544, various subclasses depending on substituents.

V. Claims 21, and 25, drawn to a method for treating heart failure, classified in classes 514, and 544, various subclasses depending on substituents.

2. Inventions of Groups I-V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated for the following reasons:

a. The method claims in groups I-V are drawn to bioassay or the treatments of disorders of different etiologies which affect different organs or tissues. Besides, the method in group I appears to be a bioassay method, and not a treatment method. The methods in groups II and III are drawn to the treatment of inflammation, osteoarthritis, or rheumatoid arthritis, which has nothing to do with heart failure or cancer. Thus, a reference anticipated the method of one group would not do so to those of the other groups. Therefore, a separate search is required for each method of treatment or bioassay which poses a burden of searching.

b. Although Groups II and III are drawn to the same methods of treatment, their compounds differ as variables R^4 , R^5 , and Ar take on different meanings, particularly non-heteroaryl vs. heteroaryl group. While both groups have the same core of

pyrimidinyl ring, said core does not define the invention because it is well known in the art. Thus, it is the combination of R⁴, R⁵ (or Ar) and the core that gives distinct physical and chemical properties to compounds of each group. Thus, the compounds in Groups II and III are patentably distinct over each other, and require an additional search which poses a burden of searching.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Groups II-V, restriction for examination purposes as indicated is proper.

3. During a telephone conversation with Mr. Claude Purchase on 10-29-03 a provisional election was made with traverse to prosecute the invention of Group II, claims 6-11 (in part), and 22-24 (in part). Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-5, 12-21, and 25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1624

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear if claims 22-24 are independent or dependent claims. Note, said claims refer to compounds of Formula I without reciting the chemical structure or definitions of variables. Thus, they are incomplete as independent claims, but it is not clear if they are dependent on claim 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 6-8, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by the following references:

a. **Nickell et. al.** (US 3,118,754): Table 1 of the reference lists several compounds (e.g., first two compounds, and the 13th compound) that fall within the scope of formulae I-III (in the instant claims 6-8) with the following substituents:

i. R² is hydrogen; E is O;

Art Unit: 1624

- ii. A and B are both $-OR^4$, wherein R^4 is hydrogen or C_1 -alkyl; or
 - iii. A and B are both $-NR^4R^5$, wherein R^4 and R^5 are both hydrogen.
- b. **Yamamoto et. al.** (cited on IDS): See compound #9c On page 1279, Table II and III;
- c. **Beilstein RN# 139954** (of document #XP002198558 cited on IDS);
- d. **Matsumoto et. al.** (CA 79:66394u) – the compound of “*dimethyl-4,6-pyrimidinedicarboxylate*”;
- e. **Sakasai et. al.** (cited on IDS): See compounds Va, and Vb;
- f. **Hunt et. al.** (cited on IDS): See the compound of “*methyl Pyrimidine-4:6-dicarboxylate*” on page 529;
- g. **Takahashi et. al.** (CA 83:178072 – also CAS printout): See the compound of *pyrimidine-4,6-dicarboxylic acid*;
- h. **Nuenhoffer et. al.** (CA 81:169499 – also CAS printout): See the compound of formula I, or *4,6-pyrimidinedicarboxylic acid, dimethyl ester* (of CAS printout);
- i. **Prikazchikova et. al.** (CA 81:100677 – also CAS printout): See the compound of *4,6-pyrimidinedicarboxylic acid* (of CAS printout);
- j. **Matsumoto et. al.** (CA 79:66394 – also CAS printout): See the compound of *dimethyl-4,6-pyrimidinecarboxylate*;
- k. **Titov et. al.** (CA 77:94976 – also CAS printout): See the compound of *4,6-pyrimidinedicarboxylic acid* (of CAS printout);

- l. **Mermann** (CA 67:69036 – also CAS printout): See the compound of 4,6-*pyrimidinedicarboxylic acid* (of CAS printout).

The compounds of references in items c-1 read on a compound of formulae I-II (in the instant claims 6 and 7) with the following substituents:

- iv. R^2 is hydrogen or alkyl; E is O;
 - v. A and B are both $-OR^4$, wherein R^4 is hydrogen, or alkyl;
- m. **Schmaizi et. al.** (EP'057 cited on IDS): the compound of Example 6 on page 7 reads on a compound of formulae I-II (in the instant claims 6 and 7) with the following substituents:
- vi. R^2 is hydroxy; E is O;
 - vii. A and B are both $-OR^4$, wherein R^4 is hydrogen;
- n. **Beilstein RN#786662** (of document XP00219556 – cited on IDS); reads on a compound of formulae I and III (in the instant claims 6 and 8) with the following substituents
- viii. R^2 is halogen; E is O;
 - ix. A and B are both $-NR^4R^5$, wherein R^4 and R^5 are both hydrogen.
- o. **Baader et. al.** (EP'797 – cited on IDS): The compound in Beispiel 2 on page 6 reads on a compound of formulae I, III, and V (in the instant claims 6, 8, and 10) with the following substituents:
- x. R^2 is hydrogen; E is O;

Art Unit: 1624

- xi. A and B are both $-OR^4$, wherein R^4 is hydrogen or C_1 -alkyl; or
- xii. A and B are both $-NR^4R^5$, wherein one of R^4 and R^5 is hydrogen while the other is $(CH_2)_n$ -aryl, and $n = 1$.

Claim Objections

7. Claim 11 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claim recites species that are not disclosed in the prior arts of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (7 am -12 pm, and 3 pm - 6 pm) starting from 10-1st -03).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Alan L. Rotman

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

T. Truong

October 31, 2003